

Non-invasive quantification of prostate cancer using AMICO framework for VERDICT MRI

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Synopsis

The aim of this study is to extend the AMICO framework to the VERDICT model-based diffusion-weighted MRI (DW-MRI) technique and to evaluate its performance to prostate cancer imaging. DW-MRI was acquired for 4 subjects and the VERDICT model was fitted to the data using both fitting procedures. In both cases similar differences in parameter values between tumour and normal tissue were found. The AMICO formulation reduces the computation time for VERDICT and produces parameter maps that are more homogeneous than those obtained with the original fitting. The AMICO formulation reflects the microstructural differences in a clinically practical time.

Abstract

Purpose

The aim of this study is to extend the AMICO¹ (Accelerated Microstructure Imaging via Convex Optimisation) framework to the VERDICT^{2,3} (Vascular, Extracellular, and Restricted Diffusion for Cytometry in Tumours) model-based diffusion-weighted MRI (DW-MRI) technique and to evaluate its performance in the clinical application for prostate cancer imaging.

Prostate cancer is the most common cancer among men in all economically developed countries⁴. A non-invasive method of diagnosis and grading would revolutionise clinical practice. VERDICT, a model-based technique, for characterising microstructural tissue parameters has shown promise in preclinical studies² and in a pilot clinical setting³ for discriminating normal and malignant prostate tissue. However, VERDICT uses a computationally expensive non-linear fitting procedure to estimate model parameters from the data, which limits its use in large cohort studies and real-time clinical applications. Recently, ultrafast fitting algorithms, such as the AMICO framework, have been developed to address the computational cost of model-based microstructure-imaging techniques. Through linearization and convex optimisation, AMICO reduces dramatically the computational cost of microstructure imaging techniques in the brain and locates the global minimum parameter values more reliably.

Methods

4 subjects suspected for prostate cancer with a previous multiparametric prostate MRI (mpMRI) were scanned for VERDICT analysis. For each subject DW-MRI was performed using a 3T scanner (Achieva, Philips Healthcare, Netherlands) using a pulse-gradient spin-echo sequence and a 32 channel cardiac coil with b values of 90-3000s/mm in 3 orthogonal directions,⁵ the imaging parameters are summarised in Table 1. Data was normalised with a b=0 image for every echo time to avoid T2 dependence. In one case (subject 4), the scan was repeated after a 2-minute interval.

MR datasets were analysed with Osirix Version 7.0 (Bernex, Switzerland). For each subject a board certified radiologist (EJ) manually contoured three regions of interest (ROIs): (1) the whole prostate, (2) a region corresponding to tumour tissue and (3) a region for normal tissue on the same slice.

The VERDICT model was fitted to the data in each voxel using both the original non-linear fitting algorithm (ORIGINALVERDICT) and the AMICO framework adapted for VERDICT (AMICOVERDICT). ORIGINALVERDICT uses an iterative optimization procedure^{2,3} that accounts for local minima and Rician noise, as implemented in the open-source Camino toolkit.⁶ AMICOVERDICT expresses the VERDICT model as a linear system and leading to a convex optimization problem, which is solved to fit the model to the data using freely available code (<https://github.com/daducci/AMICO/>).¹ Both procedures fit the same set of parameters.

The time required to fit the models to the data is compared. For subject 4 the repeatability of both models was also tested. All the experiments have been conducted on a 3.1 GHz Intel Core i7, 8 GB ram DDR3, without multi-threading or parallel computing.

Results

Subjects' ages range 62.7 to 74.4 years. In all cases a biopsy performed within a week of the scan confirmed cancer with Gleason scores⁷ of 3+4. The computation time for VERDICT is reduced with the AMICOVERDICT formulation, from 1.18s/voxel to 0.78ms/voxel, the exact time required to compute the parameter maps is reported in Table 2.

Figure 1 shows that AMICOVERDICT parameter maps are more homogeneous (less noisy) than those obtained with the original fitting. This is most likely because AMICO is less sensitive to local minima – the more homogeneous minimum objective function maps (the numerical values are not directly comparable) support this. Both models show similar differences in parameter values between tumour and normal tissue, for example, in both cases *f*_{IC} (Intracellular volume fraction) is higher and *f*_{EES} (Extracellular-Extravascular volume fraction) is lower in tumour tissue compared with normal tissue. However, the numerical values in Figure 2 show differences between the two estimation procedures, although both estimates are physiologically plausible. Both procedures provide similar reproducibility between acquisitions as illustrated in Figure 3.

Discussion

The principal benefit of the AMICO framework is that provides an acceleration factor of several orders of magnitude compared with non-linear fitting, which we demonstrate here for the VERDICT model. AMICO may also achieve more robust and repeatable parameter estimates, although further work on a larger cohort and comparison against histology is

required to test this. Improved location of the global minimum parameter values may also enable relaxation of some of the assumptions in the VERDICT model, such as fixed diffusivities and zero permeability, thus supporting more detailed and accurate microstructural assessment – future work will also evaluate this possibility.

To conclude, $_{AMICO}$ VERDICT reflect the microstructural differences between tumours and normal tissue in a clinically practical time. Results should be evaluated in larger cohorts to test the parameters correlation with cancer grade.

References

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Figures/Tables Captions

- Table 1: Diffusion MRI protocol details for VERDICT analysis.
- Table 2: Computation time required by the original VERDICT and the $_{AMICO}$ -VERDICT for each analysis in this study and the mean time per voxel.
- Figure 1: For each subject ROIs (red: whole prostate, white: tumour, orange: normal) and VERDICT maps comparison. fIC: intracellular volume fraction, R: cell radius, Cellularity: calculated dividing the fIC by the cell volume, fEES: extracellular-extravascular volume fraction, fVASC: vascular volume fraction, fobj: objective function to evaluate the measures' stability.

- Figure 2: ORIGINAL VERDICT and AMICO VERDICT parameter estimation for all voxels within the tumour and normal ROIs. Edges of the boxes define the 25th and 75th percentile range and the central mark is the median value.
- Figure 3: Subject 4 parameters estimation comparison between two different acquisitions. Estimation for all voxels within the tumour and normal ROIs for both models (ORIGINAL VERDICT and AMICO VERDICT). Edges of the boxes define the 25th and 75th percentile range and the central mark is the median value.

b value [s/mm²]	Δ/δ [ms]	TE [ms]	 G [T/m]
3000	24.7/43.8	90	0.0439
2000	13.2/32.3	67	0.0758
1500	24.7/43.4	90	0.0311
500	12.2/31.3	65	0.0415
90	12.2/23.8	50	0.0506

Table 1: Diffusion MRI protocol details for VERDICT analysis

Patient	1	2	3	4 (Acq. 1)	4 (Acq. 2)	One Voxel
Voxels	9544	2924	2746	6363	6186	
ORIGINAL VERDICT	163.52 min	56.65 min	59.48 min	122.58 min	126.91 min	1.18 s
AMICO VERDICT	7 s	3 s	2 s	5 s	4 s	0.78 ms

Table 2: Computation time required by the original VERDICT and the AMICO-VERDICT for each analysis in this study and the mean time per voxel.

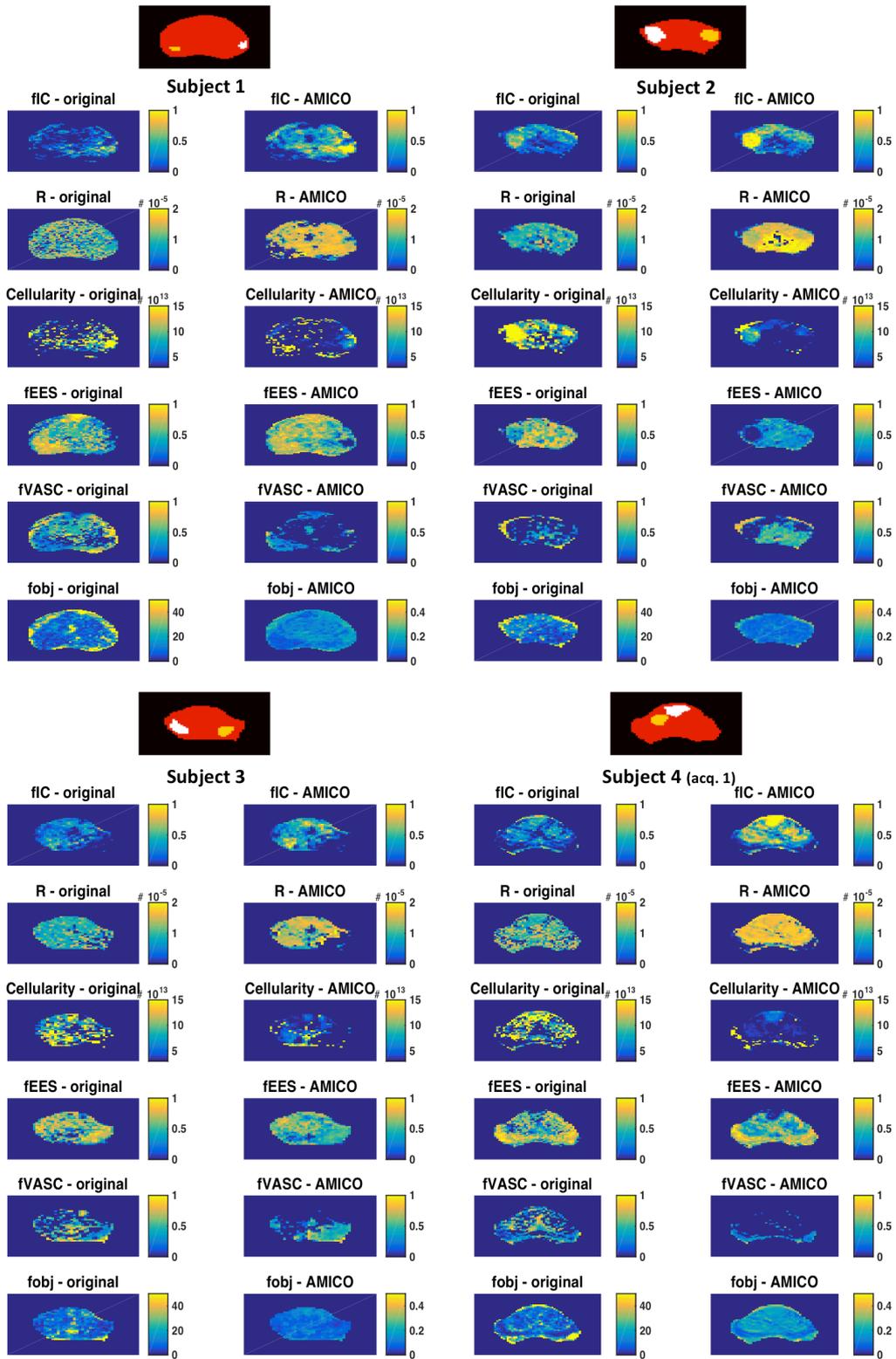


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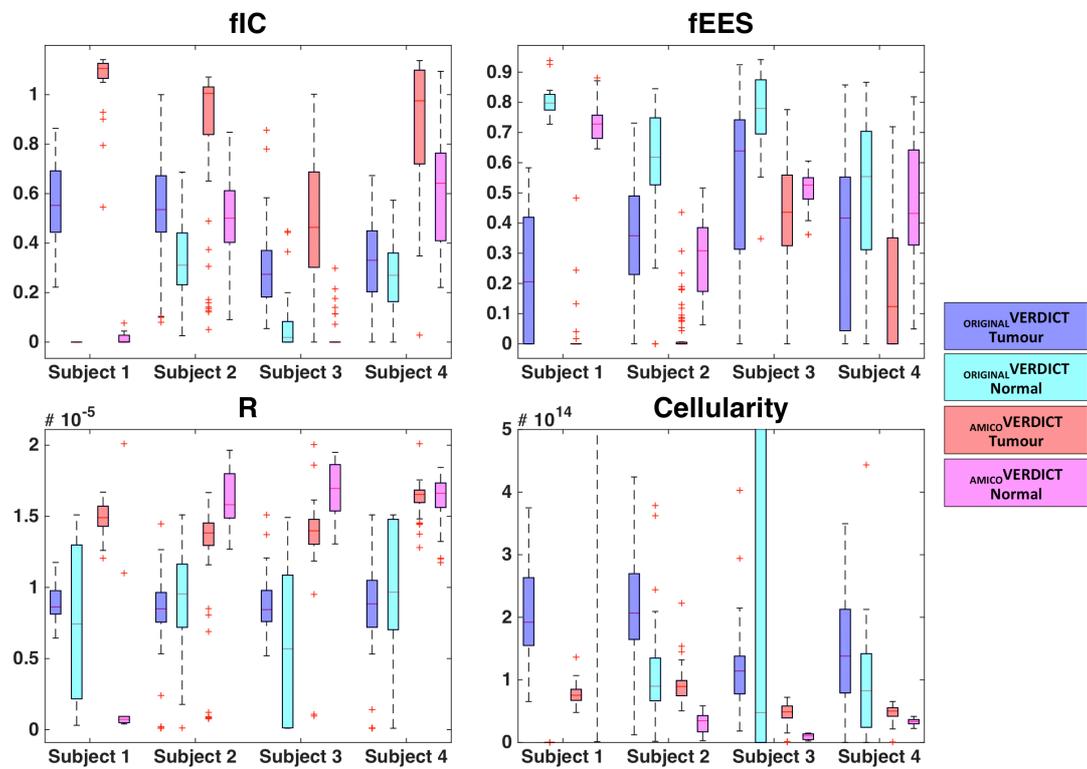


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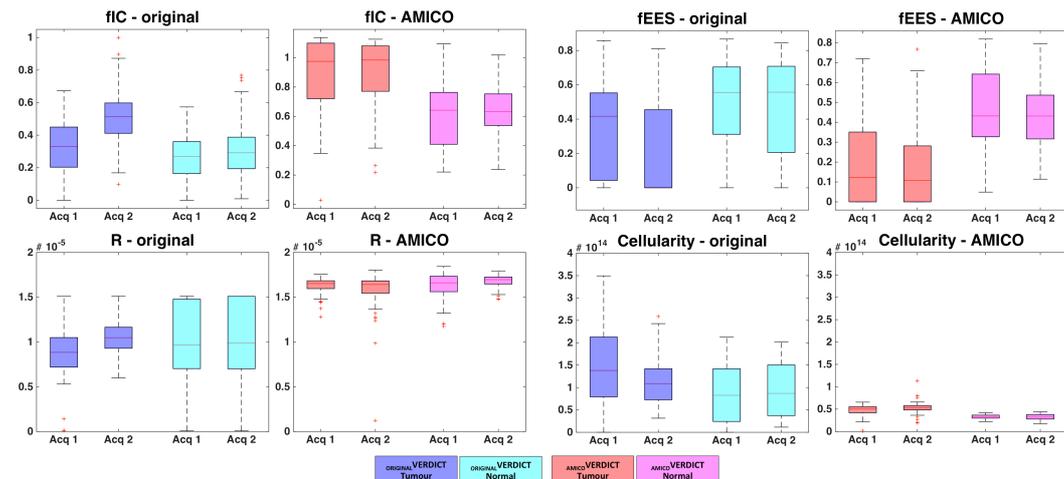


Figure 3: Subject 4 parameters estimation comparison between two different acquisitions. Estimation for all voxels within the tumour and normal ROIs for both procedures (ORIGINAL VERDICT and AMICO VERDICT). Edges of the boxes define the 25th and 75th percentile range and the central mark is the median value.